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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,600	10/28/2003	Dennis A. Steindler	7203-8	6329

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,600	STEINDLER ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response of August 14, 2006, to the non-final action dated March 14, 2006 has been entered. No claims were cancelled and no new claims were added. Claims 30, and 33-37 have been amended and remain pending in the application.

Claims 30-39 are under current examination.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 33-36 were previously rejected in the office action dated March 14, 2006, and claims 37-39 stand rejected under 35 USC § 112- Second Paragraph, as being indefinite. Applicants amendment of claims 33-37 to recite multipotent overcomes the previous ground for rejection of the claims as lacking an antecedent basis.

The rejection set forth on pp. 2-3 of the previous office action dated is maintained for claims 37-39, for reasons of record. Applicants amendment of the claims to recite *ex vivo* culture followed by introduction of the cells into a tissue in an animal subject fails to overcome the rejection, because claim 37 is directed to isolated brain stem cells. As stated in the previous office action, cells may not at once be isolated and be present in the tissue of an animal subject, because they would no longer remain isolated. Thus, the rejection of claims 37-39 is maintained for reasons of record and the foregoing discussion.

New Claim Rejections - 35 USC § 112- Second Paragraph

Applicant's claim amendments have necessitated the following new grounds of rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is unclear. The claim refers to cells that "appear as phase-bright very dense bodies and exhibit areas of very small...".It is not clear under what conditions said appearance may be observed; i.e. to the naked eye, or under a phase contrast microscope.

Claims 31-39 depend from claim 30, and have therefore been included in the rejection.

Response to Claim Rejections - 35 USC § 112, Written Description

Claims 30-39 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The rejection set forth on pp. 3-6 of the previous office action dated March 14, 2006 is maintained for reasons of record.

Applicants argue that claim 30 has been amended to recite "human and murine", and as such the rejection is moot. Applicants arguments have been fully considered, but not found persuasive. Regarding the amendment of claim 30, the previous office action set forth the reasons why the instant specification only demonstrates possession of a mixed population of human and mouse brain progenitor cells, and further stated that the term murine encompasses the species such as rat and gerbil, for which possession could not be demonstrated. Moreover, the action outlined the reasons why Applicants have failed to demonstrate possession of any isolated cell types, given that the mixed culture of brain progenitor cells represent a continuum of cell proliferation and differentiation, that is in part dependent upon culture conditions, and further, an Artisan of skill could not differentiate between Type I and early Type II cells, both of which are immunonegative for specific markers. As such, no sub-population of cells may be demonstrated as isolated.

Regarding the current claim amendments describing an isolated cell culture containing a sub-population of cells that are immunonegative for GFP, nestin and TuJ1, and appear as phase-bright dense bodies that exhibit areas of very small punctuate staining, such is not sufficient to provide a description for a specific type of brain stem cell, in the absence of any markers, in a mixed culture of cells. Additionally, as the aforementioned (Type I) cells have not been isolated, it has not been demonstrated that such cells further differentiated into the Type II and Type III cells. Further, Applicants specification states: "The different types of clones observed in the cultures described above and in the experiments described below, represent a continuum of cell

proliferation and differentiation, with the existence of both early and late type II clones...that eventually differentiate into type III clusters...The potential for numerous, undefined hematopoeitic stem cells still exists...The use of just one feature as an identification tool can occur, although it makes the recognition of the specific stem cell type rather tenuous" (lines 7-17, p. 12).

Hence, the rejection of claims 30-39 is maintained for reasons of record and the foregoing discussion.

Response to Claim Rejections - 35 USC § 112-Lack of Enablement

Claims 30-39 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The rejection set forth on pp. 7-12 of the previous office action dated March 14, 2006 is maintained for reasons of record.

It is noted that Applicants have referred to the claim rejections as rejections under scope of enablement on p. 8 of their amendment dated August 14, 2006. Such is incorrect, as the previous office action of March 14, clearly states a lack of enablement and does not set forth any enabled scope for the claims examined.

Applicants disagree with the rejection and state that the amendment of claim 30, to recite morphological and phenotypic descriptions, overcome the rejections. Citing description of the Figure legends and descriptions in the specification, Applicants allege that such disclosure "describe the isolation of these cells", and that Examples 1-3 "describe the types of purified stem cells". Applicants' arguments have been fully considered, but not found persuasive.

The instant specification describes the mixed culture of a population of cellular aggregates described as Type I, Type II and Type III (p. 7, lines 16 and 17). As set forth in the previous office action of March 14, 2006, : The specification describes the dissociation of brain tissue and subsequent propagation of the cells in suspension cultures and concludes: "some type II cells are also present in these cultures" (Example 1, last paragraph). The specification further discloses: "The different types of clones observed in the cultures described above and in the experiments described below, represent a continuum of cell proliferation and differentiation" (lines 7-8, p. 12). Examples 1, 2 and 3 of the specification further teach that the continuum of cell differentiation, is dependent in part on the cell culture conditions. The specification does not

describe either the isolation or the purification of a subpopulation of cells that may be described as either Type I or Type II and are immunonegative for the markers tested. Moreover, it is apparent from the preceding that the culture of brain stem cells contains both Type I and Type II clones. No data or evidence is presented to show that Type I clones or stem cells that are immunonegative for glial fibrillary acidic protein, nestin and TuJ1, are capable of differentiation into Type II and Type III clones. This is further complicated by the observation that upon initial culture, Type II clones are themselves immunonegative for glial fibrillary acidic protein, nestin and TuJ1. Therefore, a sub-population of multipotent progenitor or precursor stem cells giving rise to immunopositive Type II clones may in fact be immunonegative Type II clones and not Type I clones. Moreover, as the culture contains a mixed population of cells, it would not be possible to determine whether the cells giving rise to or differentiating into Type II and Type III cells are in fact Type I cells, or different stem cells present in the mixed culture or stem cells that are only viable in the brain tissue. Therefore, there is no nexus between Type I cells (clones) and Type II and Type III clones. A definitive test to show the multipotency of Type I clones, would require their purification from the mixed culture, and subsequent differentiation into Type II and Type III clones. In the absence of any known positively displayed cell surface markers, the purification of Type I clones would require additional experimentation, without any guarantee of success.

In conclusion, a mixed population of cell aggregates may not be correctly described as either "isolated" or "purified stem cells". Hence, the rejection of claims 30-39 is maintained for reasons of record and the foregoing discussion.

Conclusion

Claims 30-39 are not allowable.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Claims 30-39 are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(703) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER